The LEUCOCYTOSIS of WHOOPING COUGH

with special reference to

D I A G N O S I S

T H E S I S

Presented

to

THE UNIVERSITY OF EDINBURGH,

by

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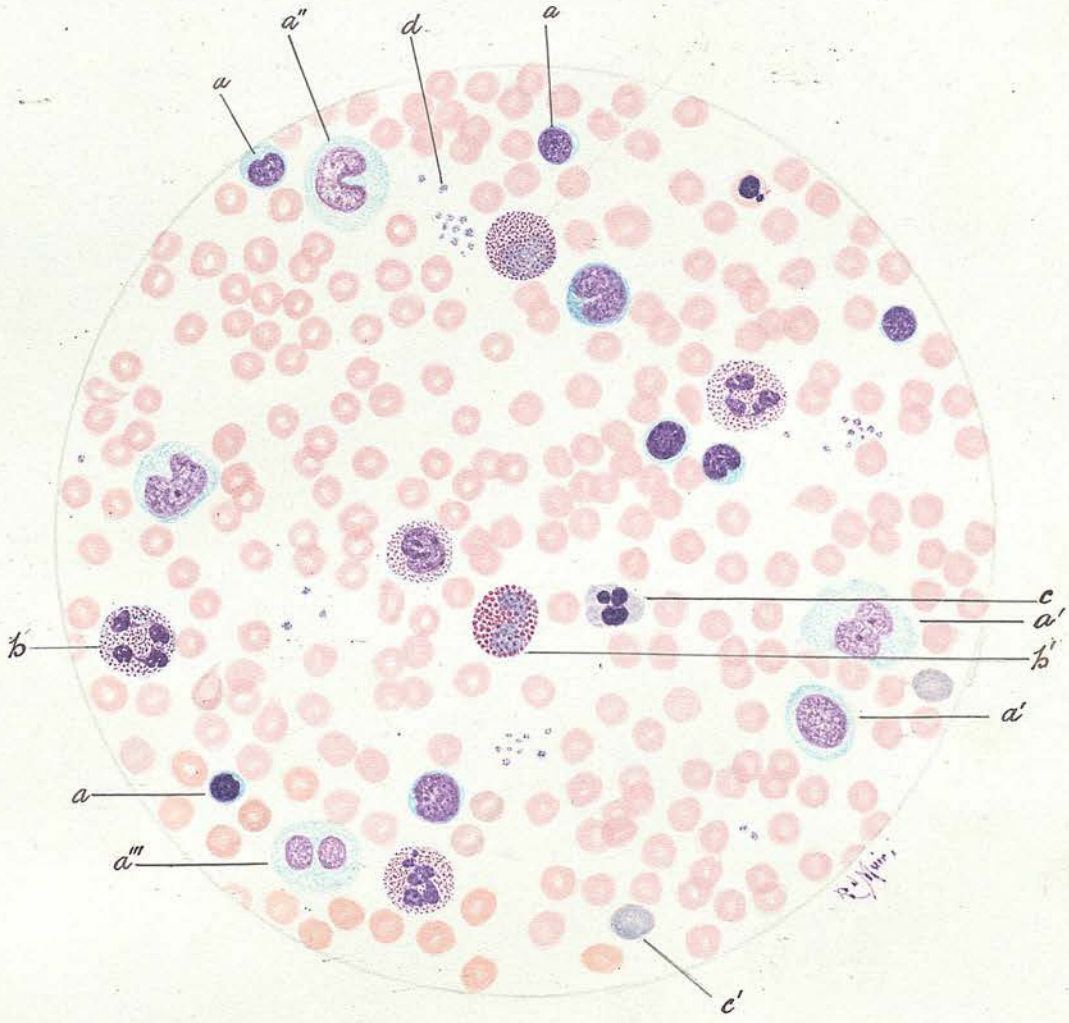

Blood Film from a case of Whooping Cough
× 500 diameters.

a — Small Lymphocyte
a' — Large Lymphocyte
a'' — Transitional form
a''' — Large Lymphocyte with double Nucleus
b — Polymorph. Leucocyte
b' — Eosinophile Leucocyte
c — Megaloblast
c' — Polychromatophilic Red
d. — Blood Plates

General Remarks:

The epidemic of whooping cough investigated began in July, 1905. It was mild in character and the schools being closed, attracted little attention so that it was not till the beginning of September, 1905, that the first cases came under my observation. I was asked to see two cases which happened to be rather more severe than the others--from curiosity I took a blood count, and in both cases was surprised to find a high leucocytosis. On inquiring into the literature of the subject I found it very scanty, and entirely foreign or American. I then decided to investigate the subject further, and the results of my researches are embodied in this thesis. Unfortunately by this time the epidemic had nearly run its course, and I was not able to investigate as many cases in the early stages as I would have wished. As it is well known that a leucocytosis is common among ill nourished and delicate children, I ought to state that all the cases were healthy, strong children with two exceptions (Nos. IV and XI) and all resided in North Berwick, and the country round about. They were children of artisans &c, all well fed and looked after, in contradistinction to the children of the outpatient Department of a hospital, or the slums of large towns from whom I think most of the figures published are obtained.

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TECHNIQUE.

To avoid digestion lencocytosis all cases were examined some hours after a meal, usually just before their dinner or tea hour. The blood was always taken from the ear as this was found to cause the minimum amount of discomfort to the patient. The ear was punctured with a Graefe's Knife, the first drop of blood wiped away, and the blood to be examined was then collected in a large bore pipette or "white-counter", and diluted, 1 - 20, with an ½% solution of acetic acid tinted with methyl green.

In drawing up the diluting fluid it is important to keep the pipette at first as nearly horizontal as possible, to roll it round and round as the fluid is drawn up, and finally to bring it to the vertical as the fluid reaches the mark 11, so as to ensure stopping exactly at the mark. The pipette must of course be perfectly dry and clean, or the result will be fallacious. The counting was done with a Thoma Zeiss counting chamber with Zappert's lines. This gives us eight undivided squares round the central divided square; the whole nine squares were counted, the product divided by 9 and multiplied by 200, giving us the number of leucocytes per cubic millimetre of blood.

Blood Films:

Blood Films:

These were in the first few cases taken entirely on coverglasses; the best results being obtained from those films that were spread by means of a strip of cigarette paper. The great majority of films were however taken on slides by a method described by Coles (1). This was found to be much preferable to using cover glasses as giving a larger area from which a workable field could be obtained, and also being easier to stain.

Coverglass specimens were however taken from every case as a control.

In making slide films the chief points to be observed are firstly, that the slides should be perfectly clean and dry, secondly, that as short a time as possible should elapse between the blood issuing from the puncture and being spread on the slide, and thirdly, that the films should be thin, and evenly spread. If the last point is not observed the leucocytes are found to be collected towards the end of the film with the Polymorphs predominating. To avoid this fallacy and also for general accuracy it is advisable in differential counting, to count the leucocytes over all parts of the film.

Staining:

All films were stained with Leishman's stain by

a /

a modified method for which I am indebted to Major Marshall I.M.S. The pure stain is allowed to lie on the films for half a minute, an equal amount of distilled water is then added, mixed thoroughly with the stain and allowed to remain for ten minutes. This is thoroughly washed off by pouring on distilled water from a drop bottle, pure distilled water is left on the film for five minutes then poured off and the slide dried quickly by shaking in the air.

By this method of staining it is specially easy to distinguish the different varieties of leucocytes.

Differential Counting.

In making a differential count a Leitz Microscope with a $\frac{1}{12}$ in. oil immersion lens and either a No. I, III, or IV eyepiece was used.

At least 600 lencocytes were counted in every case, and in the majority of cases 800 to 1,000; the larger the number counted, the less is the liability to error. In making a classification of the different varieties of lencocytes, we are at once met with the difficulty that almost every observer has adopted a classification of his own, and the nomenclature is both varied and indefinite. The following are the different classifications adopted by some of the writers on this subject. Wharton Jones (2) in 1846 recognised three varieties.

(1) /

(1) Leucocytes with fine granules.

(2) Leucocytes with coarse granules.

(3) Nucleated leucocytes without granules.

Max Schultze (3) in 1865 recognised four varieties.

(1) Small round cells with nucleus surrounded by a little clean protoplasm and non amoeboid.

(2) Larger cells with nucleus and clear protoplasm, amoeboid.

(3) Cells with many nuclei and finely granular protoplasm, amoeboid.

(4) Cells with coarsely granular protoplasm, amoeboid.

Ehrlich (4) in 1878 divided cells according to their reactions to various stains.

Hayem (5) in 1889 divided cells into three varieties.

(1) Cells with finely granular protoplasm and large nucleus and including larger cells with indented nucleus.

(2) Cells with divided nucleus and finely granular protoplasm.

(3) Cells conspicuous by their very granular appearance.

Muir (6) in 1891 published the first description of the leucocytes in the English language. He divides leucocytes into

(1) /

(1) Small lymphocytes, 6 to 7.5μ in diameter.

(2) Large lymphocytes, 7.5 to 10μ " "

(3) Coarsely granular Cells 8 to 10μ in diameter.

Metchnikoff (7) "L'Inflammation" Paris, 1892 adopts Ehrlich's classification.

Kanthack & Hardy (8) in 1894 divided cells into

(1) Oxyphile, (coarsely granular, and finely granular).

(2) Basophile, (coarsely granular, none in blood, and finely granular).

(3) Non-granular hyaline cells.

(4) Immature lymphocytes.

Coles (9) divides leucocytes into

(1) Small uninucleated leucocytes or lymphocytes 6, - 7.5μ in diameter with deeply staining nucleus surrounded by a narrow ring of protoplasm. He adds that lymphocytes considerably larger than the above are met with, and are indistinguishable from the hyaline cell.

(2) Large uninucleated leucocytes; 8.5 - 12μ in diameter; large spherical or oval cells with abundant protoplasm and nucleus often Kidney shaped or notched.

(3) Multinucleated leucocytes.

(4) /

(4) Eosinophiles.

(5) Marrow cells and Mast cells found only in pathological blood.

V. Limbeck (10) divides leucocytes into

(1) Eosinophiles; (2) Neutrophiles;

(3) Basophiles; (4) Mast cells;

(5) Marrow cells.

Cabot (11) divides leucocytes into

(1) Small lymphocytes, 5 - 10μ in diameter,

(2) Large lymphocytes, 13 - 15μ in diameter, with nucleus occupying relatively less of the cell than in the small lymphocytes and staining less deeply. In this group he includes the so-called "transitionals" and "large mononuclear leucocytes," and adds that in many cases it is quite impossible to divide lymphocytes into large and small, though we may say which predominates.

(3) Polymorphonuclear neutrophiles.

(4) Eosinophiles.

(5) Mast cells.

Ewing (12) divides leucocytes into

(1) Lymphocytes (a) Small 5 - 8μ in diameter.

(b) Large 8 - 10μ in diameter.

(2) /

(2) Large monoculear leucocytes.

(3) Polynuclear neutrophile leucocytes.

(4) Eosinophiles.

(5) Mast cells.

DaCosta (13) divides leucocytes into

(1) Small lymphocytes, 5 - 10μ in diameter, with deeply stained nucleus surrounded by a narrow rim of protoplasm.

(2) Large lymphocyte, including the large mononuclear leucocyte 11 - 15μ in diameter, nucleus round or ovoid situated towards the periphery of the cell, not staining so deeply as in the small lymphocyte and surrounded by a relatively larger amount of protoplasm. He adds that in spite of every precaution differential counts are apt to be inaccurate, so much depending on the personal equation.

(3) Transitional forms--cells resembling the large lymphocyte but with an indented nucleus.

(4) Polynuclear neutrophiles.

(5) Eosinophiles.

(6) Basophiles.

Bezancon & Labbe (14) divide what they call the non-granular, mononucleated leucocytes into

(1) /

(1) Lymphocytes, smaller than a red corpuscle with a round or slightly Kidney shaped nucleus surrounded by a narrow rim of protoplasm.

(2) Medium Mononuclear leucocytes, twice the size of a red cell; 10 - 14μ in diameter, nucleus round, oval or Kidney shaped and not so basophile as in the lymphocytes.

(3) Large mononuclear leucocytes, 15 - 20μ in diameter, nucleus excentric, round, oval or Kidney shaped. Protoplasm very pale and abundant.

(4) Transitional forms, nucleus pale and horse-shoe or Kidney shaped.

They add that the differentiation of the above varieties is often difficult.

Scott of Cambridge (15) in a classification of the cells found in the blood in health and disease has added to the confusion by dividing leucocytes into

(1) Finely granular eosinophile (neutrophile) cells.

(2) Coarsely granular eosinophile cells.

(3) Basophile cells.

(4) Hyaline cells, 10 - 11μ in diameter, nucleus irregularly oval, protoplasm forming /

forming one third of the cell and having the appearance of ground glass.

(5) Small Hyaline Cells, 8 - 9μ in diameter.

(6) Lymphocytes, 6 - 8.5μ in diameter, with round nucleus and transparent protoplasm.

Gulland (16)

In a paper on the Role of the Lymphocyte, read at the Oxford meeting of the British Medical Association in 1904, has done much to simplify the classification of leucocytes. He states that the lymphocytes, mononuclears and transitionals are merely stages in the development of one type, and that there is no relation between the transitionals and the polymorphonuclear neutrophiles or "polymorphs," He explains that the reason why the cytoplasm of the mononuclears and transitionals is less basophile than that of the lymphocyte is because there is more of it, the strands of the cytoplasmic reticulum being thinner and more widely separated in the former cells.

The depth of staining in the nucleus in different cells depends on the spacing of the chromatin in the same way as in the cytoplasm.

The deformed or indented nucleus he considers to be due to the radii of the cytoplasm pulling or attempting to pull the atrosphere to the centre of the /

the cell. In lymphocytes with a small amount of cytoplasm, the pull is not strong enough to bring this about. As the cytoplasm increases in amount the pull becomes stronger, and the nucleus is pushed to one side and becomes deformed. In large mononuclears where the cytoplasm is relatively very large in amount, the atrosphere can reach the centre of the cell without causing any deformity of the nucleus. Granules being the nodal points of the reticulum of the cytoplasm are more conspicuous in the larger cells though occurring in all.

The larger size of the mononuclears &c, depends on their taking up fluid, and the strands of the reticulum being widely separated.

A further proof of identity is that mononuclears and transitionals are found in lymph glands. Gulland, accordingly classes leucocytes as lymphocytes, neutrophiles, eosinophiles and basophiles.

Houston of Belfast, (17)

In a paper read at the same meeting at Oxford states that there is a connection between the large mononuclears and certain pathological conditions, a table of which he gives.

From those different ideas as to classification which I have described, it can easily be seen how difficult it is to decide what is the best classification to adopt, more especially if one wishes to /

to compare one's statistics with those already published, or to make them comparable with statistics that may be published in future.

The Classification which I have adopted is into

(1) Polymorphonuclear neutrophilis called polymorphs for the sake of brevity.

(2) Small Lymphocytes.

(3) Large Lymphocytes.

(4) Transitional Forms.

(5) Eosinophiles.

A few basophiles were found but not in sufficient numbers to be worthy of classification. A classification of this kind is the one I think most commonly adopted though it is by no means ideal, the great difficulty being to decide what is a large and what a small lymphocyte.

A Small Lymphocyte I consider is one with a deeply stained nucleus and relatively small amount of protoplasm, the nucleus being round or occasionally Kidney shaped.

A Large Lymphocyte is a cell at least three times the size of a red blood corpuscle with a less deeply stained nucleus, often excentric and frequently oval or Kidney shaped, the protoplasm being relatively large in amount. This closely resembles the large mononuclears of some authorities.

Transitional forms /

Transitional forms are large lymphocytes with a more or less deeply indented nucleus. As no one now-a-days believes this form to be transitional between the Polymorphs and the lymphocytes, it seems hardly worth while to keep it in a class by itself, if it were not that some authorities consider it of importance as showing a rapid increase of lymphocytes in the circulating blood.

In many cases examined, especially those with a high leucocytosis every variety of lymphocyte as regards size, shape &c was found, and to attempt to divide lymphocytes into those larger and those smaller than 8 micromillimetres in diameter was quite impossible.

I found it necessary to draw a hard and fast rule, and when in doubt as to whether a lymphocyte was large or small to class it among the latter.

In several cases with a high leucocytosis, large lymphocytes with a double nucleus were found, The various stages, in what was a division of the nucleus, could be observed, the nucleus first of all swelling up, becoming more and more deeply indented until the two halves were united by a mere shred of tissue. The two nuclei then separated and went to opposite poles of the cell.

The different varieties of cells met with in the blood of whooping cough are well exemplified in /

in the accompanying drawing, for which I am indebted to Mr Richard Muir of the Pathological Department of the University of Edinburgh. It was taken from a blood film of a child with a very high leucocytosis.

In the summary of my cases I have in addition classified the leucocytes as Polymorphs, large lymphocytes, small lymphocytes and eosinophiles, and finally adopting Gulland's classification into polymorphs, lymphocytes and eosinophiles.

We must now consider what is the normal leucocytosis and what the normal percentage of the different varieties of leucocytes in the adult and in the child.

The following table shows the average number of leucocytes per C,mm, as determined by various authorities.

Thoma	8,687
Von Limbeck	8,500
Ruder	7,680
Boeckman, Halla,	7,533
Graeber, Reinecke	7,242
Tumas	6,200
Hayem,	6,000
Average	7,406

DaCosta /

DaCosta, Cabot, Bezançon and Labbé all give the average as 7,500 per C.mm. and consider that the leucocytosis is pathological if it exceeds 10,000 per C.mm.

I will therefore take 7,500 per C.mm. as representing the normal leucocytosis in the adult.

Number of leucocytes at varying ages.

DaCosta quotes a table by Rotch (18) in Pediatries; Bezançon & Labbé (14) while giving the average at various ages state, as do all the other authorities, that the number of leucocytes varies very much in infants depending on the state of nutrition, feeding, and such slight ailments as diarrhoea &c.

Hutchison in the Lancet (19) gives a very comprehensive table.

From these authorities and others I have constructed the following table, and as my youngest case is 7 weeks old, I commence it at two months.

Age.	No. of Leucocytes per C.mm.		
2 months	11,000	1st year	11,000
3 months	12,000	2nd "	10,000
4 months	13,000	3rd "	9,000
6 months	15,000	4th "	8,000
9 months	14,000	6th "	7,500
12 months	11,000		

When we come to consider what is the normal percentage of the different varieties of leucocytes at the various age periods, we are met with the difficulty that no two authorities classify the leucocytes in exactly the same way. To overcome this I have had to adopt Gulland's classification, and to group all the lymphocytes together.

The following is a table constructed from the percentages given by the leading authorities.

	Polymorphs	Lymphocytes	Eosinophiles.
Ehrlich	70 - 72	24 - 29	2 - 4
Jolly	60	30 - 33	.5 - 5
Labbé et Bezançon	66	36	1 - 2
Hayem	62	36	.5 - 5
Cabot	62 - 70	24 - 38	.5 - 5
DaCesta	62 - 70	24 - 38	.5 - 5
average (adult)	65	32	2.5

Bezancon & Labbé state that in adults we may consider the blood to be pathological if the polymorphs exceed 70% or are less than 60%, and if the lymphocytes are more than 40% or less than 30%

The following table for Polymorphs and Lymphocytes I have taken from one given by Hutchison (19)

	Polymorphs.	Lymphocytes.
1st six months,	36	60
2nd " "	44	53
1st year	48	47

	Polymorphs.	Lymphocytes.
2nd Year	52	46
3rd "	56	42
4th "	64	34
5th "	60	38
6th " and upwards	65	32

Synopsis of Cases.

I have altogether 105 counts of 44 cases of whooping cough, and have arranged them in the following tables.

I. Cases in the catarrhal stage.

That is those cases with a cough, and who subsequently developed the characteristic paroxysmal cough or whoop. This group is naturally small in number, because one usually does not see cases till after the development of the whoop.

II. Cases during the first week of the whoop and without complications.

IIa. Cases during the first week with complications.

III. Cases during the second week of the whoop without complications.

IIIa. Cases during the second week with complications

IV. Cases during the third week without complication.

IVa. /

IVa. Cases during the third week with complications

V. Convalescent cases:--these are cases with only a slight cough and who have lost or almost lost the whoop.

VI. Chronic Cases:--those cases who have had the characteristic whoop for, from six weeks to four months.

VIa. The same cases as in No VI, the counts being taken from one to five weeks afterwards and at a time when they were all improving, with less whoop &c.

VII. Cases which never developed the characteristic whoop and which will be discussed in detail later.

VIII. Some cases with the highest counts.

IX. Some cases with the lowest counts.

X. An analysis of eight typical cases.

XI. An analysis of two cases with Bronchopneumonia.

XII. One case observed during the puerperium;

I have taken the average of each of these first nine groups and embody them in a table at the end. I have also taken the normal count of each case at the different age periods and compared them with the above.

P.M. = Polymorphs; S.L. = Small Lymphocytes;
L.L. = Large Lymphocytes; T.F. = Transitional Forms;
E. = Eosinophiles.

I.

Catarrhal Stage.

No.	Age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
I.	7wks	17,000	28	4	66.5	1	.5	Many inter-mediate forms of lymphocytes
II.	2yrs	31,300	14	7.5	76	.5	2	Cough for 2 weeks.
III.	2 "	24,200	17	7.5	73	.5	2	Cough for 2 weeks.
IV.	7 "	16,800	34.5	3	61.5	.5	.5	Cough for 2 weeks.
average		22,325	23.4	5.5	69.2	.6	1.2	
normal		9,625	-	-	-	-	-	

II.

Whoop for one Week.

No.	age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
V.	14yrs	8,000	49.5	5.5	42	1	2	Mild attack.
II.	2 "	16,100	13.5	7	76.5	1	2	
I.	9wks	12,000	24.5	5	63	5.5	2	Cough for 3 weeks slight whoop.
VI.	4yrs	20,200	40.5	2	55.5	1	1	Severe case.
VII	7 "	18,000	68	3	27	1	1	Mild case.
VIII	5 "	10,600	20	4	75	1		" "
IX.	7 "	24,800	31	4	62	2	1	Cough 2 weeks whoop 4 days severe.
X.	5 "	14,600	40	6	51	3		Cough 2 weeks whoop 4 days slight.
Average		15,535	36	4.5	56.5	2	1	
Normal		8,312	-	-	-	-	-	

IIa.

Whoop for one Week (with Complications.)

No.	Age	Leucocytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XI.	3yrs	68,800	24	9	66		1	Bronchitis
XII.	3mos	18,600	31	6	61.5	.5	1	Bronchitis
XIII	34	19,600	82	3	14	1		Confined 36 hours previously.

III.

Whoop for two weeks.

III.	2yrs	15,300	30.5	7.5	60.5	1	.5	Mild case.
IV.	7 "	19,100	16	8	74	1	1	Whoop severe.
XIV.	9 "	11,000	57.5	4	37	1.5		Mild case.
VIII	5 "	11,080	44	10	40	3	3	
XV.	2 "	13,700	28	7.5	64	.5		
XVI.	5 "	12,000	34.5	7	53.5	4	1	Mild case.
IX.	7 "	13,000	34	5	59	2		Whoop severe
X.	5 "	9,200	46.5	5	47	1	.5	Mild attack.
Average		13,047	36	7	54	2	1	
Normal		8,125	-	--	-	-	-	

IIIa.

Whoop for two weeks (with Complications)

XVII	4½	31,200	36	11	53			Bronchitis
XIII	34	8,000	46	5	48	1		Confined 10 days previously.

IV.

Whoop for three weeks.

NO.	Age	Leucocytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XII.	3mos	30,800	28.5	6.5	64	.5	.5	Severe case.
V.	14yrs	7,000	48	9	41	1	1	Mild case improving.
II.	2 "	17,600	20	4	70	1	5	Whoop severe
VI.	4 "	17,600	45.5	16	37	1	.5	Improving.
VII.	7 "	8,300	33	6	59	1	1	"
XVIII	5 "	6,500	34	5	58	3		Mild case
Average		14,633	35	7.5	55	1	1.5	
Normal		8,250	-	-	-	-	-	

IVa.

Whoop for three weeks (with complications)

XIX.	2½yrs	57,000	30	4	65		1	Bronchitis.
XI.	3 "	55,000	47	7.5	44	1	.5	"
XX.	16mos	21,400	29	11	56.5	3	.5	"
XXI.	7 yrs	5,300	45	8.5	45	1	.5	Broncho-pneumonia.

V. /

V.

Convalescent Cases.

No.	Age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XXII.	5yrs	12,200	68.5	3	28		.5	Whoop for 4 wks now slight.
XI.	3 "	13,800	38	11	60	1		Whoop for 3 mos. slight
XII.	14wks	13,600	10.5	8	81	.5		Whoop for 1 mth slight.
VI.	4yrs	9,800	46	6	43	2	3	Whoop for 5 wks slight
VII.	7 "	8,300	34	5	59	1	1	Whoop for 3 wks slight
XIV.	9 "	10,000	35	6	54.5	3	1.5	No whoop.
XXI.	8 "	6,400	38	13	46	3		" "
III.	2 "	10,200	19	12	69			Has chicken pox, slight whoop.
XXIII	3 "	10,200	29	5	63	2	1	No Whoop.
XVII.	4 "	11,800	52	7	39	1	1	Whoop for 2 mos, now slight.
II.	2 "	12,600	27	5	58	4	6	Whoop for 2 mos, now slight.
XXIII	1 "	17,760	29	4	64	1	2	No whoop.
VIII	.5 "	7,700	60.5	5	33	1	.5	
XXV.	5mos	10,000	17	8	74	1		No cough or whoop for a month
XXVI.	9 "	12,000	19	7	72	1	1	Whoop for 3 mos, now slight.
Average		11,158	34.8	7	56.2	1.4	1.2	
Normal		9,566	-	-	-	-	-	

VI.

Chronic Cases.

No.	Age	Leucocytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XXIII	1yr	14,600	12	8	79		1	*Cough 8wks Whoop 6wks.
XXVII	7yrs	13,800	47	10	40	1.5	1.5	Cough 8wks Whoop 5wks.
XXVI	9mos	19,200	21	16	59	4		Cough 1mth Whoop 2mth.
XXVIII	5yrs	18,200	74	4.5	20		1.5	Whoop 3½mths
XXIX.	3½"	14,200	50	10	34	1	5	Whoop 3 mths
XXX.	2 "	14,000	73	3	24			" " "
XXXI.	3½"	11,800	27	9	58			Whoop 3½mths
XXXI.	3½"	15,800	55	9	34		2	" " "
XXII.	3 "	13,400	27	8	62	2	1	Whoop 6wks
XVII	4 "	23,200	62	5	32		1	Cough 4 wks Whoop 9 wks
II.	2 "	13,200	28	6	64	1	1	Whoop 7 wks
XXXII	2½"	12,200	34	3	57	1	4	Whoop 4 mths
XXXIII	3½"	10,600	34	3	55	2	6	Whoop 3 mths
XXXIV	5 "	16,200	63	5	29	1	2	" " "
XXXV.	2 "	26,900	41	7	50		2	Cough 2 mths Whoop 6 wks.
Average		14,886	43	7.1	46.5	1	2.4	
Normal		8,700	-	-	-	-	-	

* Cough means duration of cough before commencement of whoop.

VIa.

Chronic Cases.

Same cases as table VI, but all now improving.

No.	Age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XXIII	1yr	11,760	21	9.5	67	1	1.5	
XXVI.	7yrs	11,800	43	3	52		2	
XXV.	9mos	12,800	34	3	62	1		
XXVII	5yrs	11,600	35.5	7	55	.5	2	
XXVIII	3½"	9,400	41	4	42	2	11	
XXIX.	2 "	9,400	43	5	48	1	3	
XXX.	3½"	7,600	35	4	56	1	4	
XXII.	3 "	10,200	29	5	63	2	1	
XVII.	4 "	11,800	52	7	39	1	1	
II.	2 "	12,600	33	8	54	2	3	
XXXIV	2 "	13,000	53	5	40		2	
Average		11,082	38.1	5.5	52.5	1	3	
Normal		9,727	-	-	-	-	-	

VIb.

Relapsing Cases

XXXV.	3yrs	17,600	55	8	35	1	1	Whooping cough 3mos Relapse 3wks ago.
XXXV.	3 "	11,800	41	7	50	1	1	Same case improving whooping Cough 2 mos.
XII.	4mos	16,000	20	12	64	4		Relapse with Bronchitis.
XII.	5mos	10,000	18	7	74	1		Second relapse

VII.

Cases without the characteristic Whoop.

No.	age	Leucocytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XXXVI	5yrs	11,200	61	9	29		1	Cough 8 wks
XXXVI	5 "	10,600	37	6	53		4	Cough 13 wks
XXXVII	10"	16,600	36	8	54	1	1	Cough 3 wks.
XXXVII	10"	16,400	66	5	26	2	1	
XXXVIII	16mos	57,800	33	5.5	58.5	2	1	Cough 2wks acute bronchitis 1 basophile and some nucleated reds.
XXXVIII	16 "	85,600	44	8	40	8		Broncho - pneumonia died following day.
XXXIX	7yrs	11,000	46.5	7.5	43		3	Cough 2 wks.
XXXIX	7 "	5,000	52	6	40		2	Much better.
XL.	7 "	18,400	81	6	11	1	1	Cough 3 wks.
XLI.	3 "	10,500	60	9	31	1		" " "
XLII.	5½"	12,400	57	10	30	3		" " "
XLIII	3½	11,300	48	13	27	2		Cough 2 wks.

VIII.

Cases with Highest Count.

XIX.	2½"	57,000	30	4	65		1	Whoop 3 wks Bronchitis.
XI.	3 "	68,000	24	9	66		1	Whoop 1 wk Bronchitis.
XIII	3mos	30,800	28.5	6.5	64	.5	.5	Whoop 3 wks.
XVII	5yrs	31,200	36	11	53			Whoop 2 wks Bronchitis.
XXXVIII	1"	57,800	33	5.5	58.5	2	1	Catarrhal stage Bronchitis.
Average		44,960	30.5	7.2	61.3	.5	.7	
Normal		9,900	-	-	-	-	-	

IX.

Cases with Lowest Count.

No.	Age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
V.	14yrs	8,000	49.5	5.5	42	1	2	Mild case
XIV.	9 "	11,000	57.5	4	37	1.5		" "
VIII	5 "	10,000	20	4	75	1		" "
XVI.	5 "	12,000	34.5	7	53.5	4	1	" "
Average		10,400	40.4	5.1	51.9	2	.6	
Normal		7,500						

X.

Some Illustrative Cases.

II.	2yrs	31,300	28	4	66.5	1	.5	Cough 2 wks No whoop.
		16,100	13.5	7	76.5	1	2	3 wks later Whoop 1 wk.
		17,600	20	4	70	1	5	Whoop 3 wks.
		13,200	28	6	64	1	1	Whoop 6 wks.
		12,600	33	8	54	2	3	Only slight Whoop.
		9,800	45	4	49	2		No whoop for 2 months.
III.	2yrs	24,200	17	7.5	73	.5	2	Cough 2 wks no whoop
		15,300	30.5	7.5	60.5	1	.5	Whoop 2 wks.
		19,900	36	8	55	1		Slight whoop
		10,200	19	12	69			Slight whoop has chicken pox
		10,000	56	4	40			Quite well for 2½mths.

No.	Age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
IV.	7yrs	16,800	34,5	3	61.5	.5	.5	Cough 2 wks delicate girl
		19,100	16	8	74	1	1	Whoop 2 wks.
		11,800	37	12	29	2		Whoop 3 wks severe. died 3 mos later from Tubercular Peritonitis
XIX.	2½	57,000	30	4	65		1	Whoop 3 weeks Bronchitis
		17,800	44	14	40	1	1	Whoop 6 weeks No Bronchitis
		16,200	72	4	24			Whoop 9 weeks improving.
XI.	3 "	68,800	24	9	66		1	Severe whoop 6days Bron-chitis.
		55,000	47	7.5	44	1	.5	Whoop 16days Bronchitis less
		40,600						Whoop 25 dys, no Bronchitis.
		21,300	43	6	49	2		Whoop 37 days, inproving
		13,800	38	11	50	1		Three weeks later, still has slight whoop.
		15,000	50	4	46			No whoop for 2 months, de-licate child
XVII	4½	31,300	36	11	53			Cough 4 weeks Whoop 2 wks Bronchitis.
		31,500	48	5	46	1		Whoop 3 weeks no Bronchitis
		18,200	48	7	45			Whoop 5 weeks
		23,200	62	5	32			Whoop 9 weeks
		11,800	52	7	39	1	1	Much better 4 wks later.
		9,600	72	3	25			No whoop for 2 months.
VIII	5 "	10,600	20	4	75	1		Cough 3 weeks Whoop 1 week
		11,080	44	10	40	3	3	Whoop 2 weeks
		11,600	47	4	47	1	1	Improving
		7,700	60.5	5	33	1	.5	Well, mild case

No.	Age	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	E.	Remarks.
XXXIV	2yrs	13,700	28	7.5	64	.5		Cough 2 mths Whoop 2 wks.
		14,800	40	7	51.5	1	.5	Whoop severe Bronchitis.
		26,900	41	7	50		2	Whoop severe Bronchitis.
		13,000	53	5	40		2	Whoop slight No Bronchitis

XI.

Cases with Broncho Pneumonia.

XX.	7yrs	5,300	45	8.5	45	1	.5	Cough 6 weeks whoop 3 wk severe Broncho-pneumonia very ill and collapsed.
		3,100						Very ill died 4 days later
XXXVIII	16ms	57,800	33	5.5	58.5	2	1	Cough 2 weeks severe Bronchitis
		85,600	44	8	40	8		5 dys later, Broncho pneumonia; died following day. a few nucleated reds were found

XII.

Cases observed during the puerperium.

No.	Age	Erythro-cytes.	Leuco-cytes.	P.M.	L.L.	S.L.	T.F.	Remarks
XIII.	34	4,608,000	19,600	82	3	13	1	Cough 3 wks whoop 3 dys, severe. Confined 36 hrs previously.
		4,584,000	8,000	46	5	48	1	8 days later. much better.

Resume of average counts of each group.

	Leucocytes.	P.M.	L.L.	S.L.	T.F.	E.
I. Catarrhal 4 cases	22,325	23.4	5.5	69.2	.6	1.2
II. First week 8 "	15,535	36	4.5	56.5	2	1
III Second Week 8 "	13,047	36	7	54	2	1
IV Third week 6 "	14,633	35	7.5	55	1	1.5
V. Convalescent 15 "	11,156	34.8	7	56.2	1.4	1.2
VI. Chronic cases 15 "	14,866	43	7.1	46.5	1	2.4
VII. Chronic cases Improving	11,082	38.1	5.5	52.5	1	3
VIII Highest Count (5 cases)	44,960	30.5	7.2	61.3	.5	.7
IX Lowest Count (4 cases)	10,400	40.4	5.1	51.9	2	.6

	Leucocytes	P.M.	*L.L.&T.F.	S.L.	E.
I.	22,325	23.4	6.1	69.2	1.2
II.	15,535	36	6.5	56.5	1
III.	13,047	36	9	54	1
IIV.	14,633	35	8.5	55	1.5
V.	11,158	34.8	8.4	56.2	1.2
VI.	14,866	43	8.1	46.5	2.4
VII.	11,082	38.1	6.5	52.5	3
VIII.	44,960	30.5	7.7	61.3	.7
IX.	10,400	40.4	7.1	51.9	.6

* Large Lymphocytes and transitional forms in one group.

	Whooping Cough.			Normal.		
Tables	Leucocytes	P.M.	L.	Leucocytes	P.M.	L.
I.	22,325	23.4	75.3	9,625	51	46
II.	15,535	36	63	8,312	58	39
III.	13,047	36	63	8,125	60	37
IV.	14,633	35	63.5	8,250	57	30
V.	11,158	34.8	64.6	9,566	55	42
VI.	14,866	43	54.6	8,700	55.5	42.5
VII.	11,082	38.1	59	9,727	55	42.5
VIII.	44,962	30.5	68.5	9,900	51	46
IX.	10,400	40.4	59.4	7,500	62	35

LITERATURE.

The following is a resume of all the literature on this subject which I have been able to discover and I think it includes, practically, all that has been written.

Frohlich (20) in 1897 is the first to mention that a leucocytosis is found in cases of whooping cough. He examined 55 cases and found a constant leucocytosis, in 32 of the cases exceeding 20,000 per C.mm. The number was highest in the third and fourth weeks of the disease when the fits of coughing were at their worst.

Meunier (21) in April 1898, has given the best and most complete description of this condition as yet published. His observations were founded on 102 counts from 30 cases of undoubted whooping cough. He states that "the leucocytosis is very high and always much higher than that which is observed in other non-febrile affections of the respiratory system, and that it appears to be due to a specific reaction bound up with the infection of whooping cough.

It appears early, rapidly reaches its height and diminishes irregularly as the disease lessens; its complete disappearance does not occur until the cessation of the recurrent fits of coughing. This leucocytosis /

leucocytosis is relatively and absolutely more intense in young children, especially in those from 2 to 3 years old, and is a little less marked in those from 4 to 7, though even at that age it is twice or thrice the normal number. The leucocytosis during the convulsive period is so high that it is unnecessary to make allowance for the age of the child. The average count is 27,800 per C.mm. instead of the normal 8,000 to 13,000. During the first week of the whoop the average is 25,500, the highest being 51,150, several being above 40,000 and the lowest, 15,500. These are all afebrile, uncomplicated cases, but even febile complications such as broncho-pneumonia &c, exercise only a slight affect and subsequent complications such as tubercular affections have not increased the leucocytosis. The increase of the white corpuscles is chiefly due to the lymphocytes and several counts made from children aged 3 years give the following figures which are contrasted with the normal for that age.

		Whooping Cough	Normal.
Lymphocytes		53.8	39
Leucocytes	Intermediary	6.4	6
	Polynucleated	39	54
	Eosinophiles	.8	1

The proportion of lymphocytes and polynucleated leucocytes is thus inverted.

We /

We find that in cases giving a leucocytosis of 30,000 instead of 10,000 that the lymphocytes are more than quadrupled, the intermediary leucocytes tripled, the polynucleated doubled, while the eosinophiles remain stationary.

Can this lymphocytosis be due to the hyper-activity of the tracheo-bronchial glands which is usually present in those suffering from whooping cough? So far from want of proof this is difficult to affirm.

In conclusion the constancy of the leucocytosis of whooping cough, the disproportion it presents with that which is noticed in other affections resembling whooping cough, (bronchitis, tracheo-bronchitic adenopathy, and pseudo whooping cough), and its early appearance, give it a real importance in cases of doubtful diagnosis and cause it to be of great value as a prophylactic in hospitals and schools."

De Amicis & Pacchioni (22) in 1899 found a leucocytosis in the blood of whooping cough patients, which reached its maximum in the spasmodic stage. It is chiefly at the expense of the lymphocytes, begins in the first days of the disease and may be prolonged for some time after the cessation of the typical paroxysms.

In /

In no other disease of the respiratory passages is a similar or so marked a leucocytosis found. The constancy of this feature of the disease suggests it as a valuable aid in early diagnosis when prophylaxis may yet be possible. The important part played by the leucocytes indicates a very active participation of the tracheo-bronchial lymphatic system.

Stengel & White (23) in 1901 found an invariable lymphocyte increase but did not find such a high leucocytosis as the preceding authorities. They give details of these cases.

	Age.	Leucocytes.	P.M.	Mononuclears	Lymphocytes	E.	Mylocytes
M.G.	22mos	12,145	40.8	27.8	24	5.6	1.8
X.Y.	4 yrs	34,667	29.2	17.4	52.6	.8	.1
T.W.	?	16,218	41.4	19.5	36.9	2.2	

	Remarks.
M.G.	Catarrhal stage.
X.Y.	Paroxysmal stage.
T.W.	Paroxysmal stage.

They state that the lymphocytes varied greatly in their characters and size; and that differentiation was difficult. They attribute the Lymphocytosis to probable disease of the tracheo-bronchial lymphatic glands.

Carrière (24) in 1902 says whooping cough is characterised /

characterised by a marked increase of the Polynuclear elements, varying from 85% in the catarrhal stage to 70% during convalescence, and that the eosinophiles vary from 12 to 15%. He considers that complications increase the leucocytosis and that in severe cases it is diminished.

Quain's Dictionary of Medicine 1902, states that a lymphocytosis with some leucocytosis is present in the catarrhal stage of whooping cough

Wanstall (25) in 1903 found in eight cases of whooping cough in the catarrhal stage, the leucocyte count to vary from 4,228 to 34,667 giving an average of 13,315. In eighteen differential counts all but three show a higher percentage of mononuclear than of polynuclear leucocytes; the average being Polynuclear 41.4% and mononuclear 55.4%. He considers that an increased percentage of lymphocytes at least equalling or exceeding that of the polynuclear leucocytes is a valuable diagnostic aid in whooping cough before the characteristic symptoms make the diagnosis easy.

Koplik (26) of New York, in 1903 states that a leucocytosis of the polynuclear type is usually present in the second week of whooping cough.

Chalmers Watson (27) quotes Cima as finding a leucocytosis /

leucocytosis in all well marked cases of whooping cough.

Grulée & Phemister (28) in 1905 investigated 15 cases of whooping cough and found a leucocytosis of from 12,500 to 48,500 per C.mm. present in all stages of the disease and varying directly with the frequency and severity of the paroxysms. The mononuclear leucocytes were relatively increased in all stages of the disease. They found the leucocytes to be present in the catarrhal stage, most marked in the paroxysmal stage and then gradually to disappear.

In one case reported in the paroxysmal stage the large lymphocytes predominated, and in one case in the catarrhal stage the small lymphocytes were in excess.

Boston (29) of Philadelphia in 1905 states that whooping cough is the only example of an afebrile disease affecting the respiratory tract where decided leucocytosis is a constant symptom. The degree of leucocytosis is influenced by the age of the child and is found to range from 20,000 to 40,000 per C.m. in uncomplicated cases during the active stage.

The lymphocytes may range from 35 to 55%, the polynuclear cells are relatively decreased and the eosinophiles are normal or diminished.

The /

The haemoglobin and red cells bear no direct relation to the degree of leucocytosis.

The International Clinic (30) 1905 says "recent studies of the blood confirm the occurrence of a lymphocytosis in whooping cough. This is found even in the early stages of the infection and may be regarded as a diagnostic sign of value."

DaCosta (31) remarks that a lymphocytosis generally relative but sometimes absolute is a characteristic finding in whooping cough. He quotes Meunier and other authorities in support of this, corroborating their views and adding "The fact that a marked lymphocyte increase occurs in the early catarrhal stages of the disease antedating the development of the typical cough is of diagnostic value."

Cabot (32) gives the following cases as corroborating Meunier's researches.

	Age	Leucocytes.	P.M.	L.	E.	Date.
I.	3yrs	75,000	42	57	1	July, 23rd
	" "	26,500				August, 19th
	" "		56	43	1	August 31st.
II.	5yrs	32,800		69		

In 1894 he had a case of Broncho-pneumonia complicating whooping cough in a girl of six whose blood /

blood conditions were entirely different from those he had previously met with in pneumonia and it was only after reading Meunier's paper that he understood how this change was due to the presence of whooping cough. This case had on admission a leucocytosis of 72,100 which two days later was 94,600 with 60% of Small Lymphocytes and 30% of Polymorphs.

Bezancon & Labbe (33) point out that we must not be misled by the differential counts in young children who normally have a high percentage of lymphocytes. They consider that the large mononuclears are the diagnostic feature in the blood of whooping cough and that they are usually present in larger numbers than indicated by Meunier. They add, however, that recent observations by Pepin show the large mononuclears to be diminished or absent.

Out of the large number of textbooks on Medicine and the Diseases of children published in this country I can only find one or two making any reference to the presence of leucocytosis in whooping cough, while all are agreed on the great difficulty of early Diagnosis.

As far as I am aware no statistics on this subject have been published in this country.

COMMENTS ON CASES

and on the

LITERATURE.

I now propose to go more fully into the cases detailed in the preceding tables, and to compare my results with those of others.

Leucocytosis :-

Dealing first of all with leucocytosis, I find that this is highest in the Catarrhal Stage, differing from the observations of Frohlich, Meunier &c. Wanstall (25) found in 8 cases in the catarrhal stage the leucocyte count to vary from 4,000 to 34,600 per c.mm. giving an average of 13,000. I find in 4 cases (Table I) all severe, the count to vary from 16,000 to 31,000 giving an average of 22,325 while the average normal count making allowance for the age of the cases would have been 9,625. Wanstall's lower average is probably due to the larger number of cases observed.

In 8 cases observed during the first week of the whoop (Table II) we find the leucocyte count to vary from 8,000 to 24,800, the mildest cases being those with the lowest count, the severest cases having the highest count. The average is 15,500, while the normal average would be 8,300.

In /

In 8 cases observed during the second week of the whoop, (Table III) we find the count to vary from 9,000 to 19,000, the mildest cases again showing the lowest count though we have here a mild case, age 2, giving a leucocyte count of 15,200. The average is 13,000 and the normal 8,000.

In six cases observed during the third week of the whoop, (Table IV) we have 6,500 as the lowest count and 30,800 as the highest giving an average of 14,000 contrasted with a normal of 8,000. Here the three lowest counts can not be called pathological and were those of mild cases which were rapidly getting better.

The highest count was that of an infant 3 months old, with a severe attack. Hayem (5) has said that the blood count of children under one year of age cannot be relied upon, and if we were to exclude this case the average count would be much lower.

In table V, Convalescent cases, I have counts of 15 cases, some of them later counts of cases noted in the previous tables. To each case I have given a number, and the same number being retained all through enables us to easily identify each case should it appear in different tables.

Here the counts vary from 6,400 to 17,700 with an /

an average of 11,100, not much above the normal of 9,500. All these were counts made of cases which were improving and had lost or almost lost the characteristic whoop. We note here that in these cases the leucocyte count is much lower than during the paroxysmal acute stage though only in one or two has the count dropped to normal. The leucocyte count does not necessarily return to normal when the characteristic whoop disappears, as the cases with the highest count in this group had been free from whoop for nearly a week.

In these five tables we have traced the leucocytosis of uncomplicated whooping cough from its commencement to convalescence, and we find that it is highest in the catarrhal stage and gradually diminishes as the cases approach convalescence. Wanstall, (25) has said in discussing this subject that the figures are more convincing in the aggregate than when considered individually. As I will show later on, this ratio holds good even in individual cases. This leucocytosis however is not met with in every case, as No V a strong, healthy girl of 14, with a mild attack gave a practically normal leucocyte count throughout.

Severe cases were found to have a much higher leucocyte count than mild cases. Frohlich (20) says the number of leucocytes was highest in the third and /

and fourth weeks of the disease when the fits of coughing are at their worst. This was not my experience as I find the average counts in the first three weeks of the disease, in uncomplicated cases, to be much the same. You may, however, get individual cases in all three groups showing a high leucocytosis on account of the severity of the symptoms; in a mild epidemic such as the one investigated, many of the cases were found to be at their worst during the first ten days.

I can corroborate the statement of Grulée & Phemister (28) that the leucocytosis varies directly with the frequency and severity of the paroxysms.

Meunier (21) says that the leucocytosis diminishes irregularly as the disease lessens, and its complete disappearance does not occur until the cessation of the recurrent fits of coughing. An examination of table V will bear this out, some of the cases showing no leucocytosis, and some, in young children, if we allow for the age, being only slightly above the normal. One case, XXIII, however still showed a considerable leucocytosis though there was no whoop. We can thus say that the leucocytosis diminishes rapidly during convalescence, and in mild cases becomes normal soon after the cessation of the whoop, but in severe cases it may persist for a considerable time after the cessation of the whoop /

whoop.

In table VI we have an analysis of 15 chronic cases who have all had whooping cough for over three months, and who have had the characteristic paroxysmal fits of coughing for from 6 weeks to 4 months. This table exemplifies the fact that there is a leucocytosis as long as the whoop lasts, and that it may persist for months. One case with a leucocytosis of 26,900 had suffered from whooping cough for 3½ months with whoop for the previous 6 weeks, while one of 23,200 was a case of 3 months duration with whoop for the previous 9 weeks.

The average for the 15 cases is 14,800 as compared with a normal of 8,700.

In table VI we have an analysis of 11 of the preceding cases which were improving. This shows how the leucocytosis diminishes as the case approaches convalescence.

The average here is 11,000 compared with a normal of 9,700, and is practically the same as that of the convalescent cases in table V.

Table VIB gives us an analysis of two cases which after being apparently well, relapsed with a recurrence of the fits of whooping &c. The second relapse in case XII was probably not a genuine one as there was no leucocytosis.

Table VII, (Cases without the characteristic whoop) I will discuss later under diagnosis.

In /

In table VIII we have an analysis of the five cases which were found to have the highest count; all but one were complicated with bronchitis, and we get an average of 44,900 instead of the normal 9,900.

In table IX we have an analysis of four mild cases giving an average of only 10,400 instead of the normal 7,500.

In table X we have a number of individual cases in whom successive counts were made from the time of their first coming under observation. They show how the leucocytosis diminishes, in some cases very rapidly, as the case progresses towards convalescense. In several cases I found it did not entirely disappear until fully two months after the cessation of the whoop. The diminution was not in all cases quite regular as occasionally a leucocytosis which was getting less was found to be suddenly increased, possibly the result of some unnoticed complication.

The influence of various complications on the leucocytosis will be considered later.

DIFFERENTIAL COUNTS.

We must now consider the effect of whooping cough on the differential count of the leucocytes. An examination of the preceding tables will at once convince /

convince us that there is a very remarkable divergence from the normal conditions at every stage and consisting in an absolute or relative increase of the lymphocytes over the polynuclear elements. This is most noticeable in the Catarrhal stage (Table I) where we have an average of 23% of Polymorphs, and 75% of Lymphocytes, instead of the normal, corrected for age, of 50% of Polymorphs, and 46% of Lymphocytes. Before deciding whether a differential count is pathological or not, we must always take into consideration the age of the patient, bearing in mind the fact that in children under one year old the Lymphocytes are normally in excess of the polymorphs. In whooping cough we find this normal lymphocytosis of children to be much exaggerated. Case II Table I, a child two years old shows a ratio of 14% of Polymorphs to 80% of Lymphocytes, and Case III, also 2 years old, is very similar; the normal count for 2 years according to Hutchison being 52% Polymorphs and 46% Lym - phocytes.

Table II gives us an average of 36% of Polymorphs, and 63% of Lymphocytes compared with the normal 58% and 39%.

Case II, 2 years old, has a ratio of 14% P,M. and 84% L. and Case VIII, age 5, 20% and 80%. In all these cases the Lymphocytes exceed the Polymorphs, except in Case VII, where the differential count /

count is practically normal though there is a decided leucocytosis. Later counts made of this case Table IV showed a relative increase of the lymphocytes. In case V, a healthy girl of 14 with a mild attack we find the lymphocytes almost equalling the polymorphs, though there is no leucocytosis.

In table III we find the average ratio of polymorphs to lymphocytes the same as in table II. A severe case, age 7 has 83% of lymphocytes while a mild case age 9 shows a percentage of 42.

In cases during the third week of the whoop, Table IV we find a similar condition of things. Case VI which during the first week of the whoop had 68% of polymorphs now has only 33%.

In cases during convalescence, table V we find the average percentage of Polymorphs to Lymphocytes much the same as during the paroxysmal stage though the leucocytosis is considerably less.

In only two cases XXII and VIII do we find the polymorphs approaching the normal.

In examining the counts of Chronic cases, table VI, we find an average of 43% P.M. and 54% L. contrasted with the normal 55% and 42%, the ratio being inverted. These cases had all suffered from whooping cough for some months and we cannot expect to find the same consistent excess of lymphocytes as in the paroxysmal stage, yet in the aggregate we do find this excess. Case XXIII for instance shows only 12% of polymorphs and 87% of lymphocytes while only

4 cases out of 15 show a percentage of polymorphs exceeding that of the lymphocytes. In the next table, (VIa) we find on examining these four cases at a later date, that they all, though improving, show a higher percentage of lymphocytes than previously and the average of all the cases in this table is 38% P.M. and 59% L. The Relapsing cases (table VIb) resemble those in the paroxysmal stage.

It is interesting to contrast tables VIII and IX; in the former, cases with the highest leucocytosis we find an average of 30% P.M. and 68% L, with a normal figure of 51% and 46%, and in the latter, cases with the lowest count we find 40% P.M and 59% L. with a normal of 62% and 35%.

It would thus appear that the cases with the highest leucocyte count show the highest percentage of lymphocytes, but this is not so, as allowing for the variation due to age, we find the differential count of the two groups almost exactly the same. It should be noted however, that four out of the five cases in Table VIII were suffering from Bronchitis which tends to cause an increase of polymorphs.

In table X we have a record of a series of consecutive counts made in individual cases.

In case II we notice that the lymphocyte percentage is highest during the first week of the whoop /

whoop and then gradually drops, though two months after the cessation of the whoop it is still above normal, 55% instead of 46%. This was a robust child, 2 years old, with a moderately severe attack.

In case III we find the highest percentage of lymphocytes during the catarrhal stage, 81% and gradually decreasing until during the convalescent stage when it is found to suddenly rise to the former figure, 81%, with an increase also of the large lymphocytes. This sudden lymphocyte increase was probably due to an attack of Chicken Pox, which the patient contracted at this time, causing an irritation of the lymphatic glands.

Two and a half months after the cessation of the whoop the number of lymphocytes was found to be normal.

In case IV the percentage of lymphocytes was highest during the second week of the whoop. This was a delicate girl who died three months later from Tubercular Enteritis and Peritonitis. The last count made of this case shows a leucocytosis of 11,800 with 12% of large and 29% of small lymphocytes. This corroborates Meunier's observation that subsequent complications such as tubercular affections do not raise the leucocytosis. The unusually high percentage of large lymphocytes may be the result of the tubercular condition of the abdominal glands.

Case /

Case XIX is only remarkable for the fact that the differential count returned to normal before the cessation of the whoop, and while there was still a leucocytosis. This was quite exceptional and occurred in only one other case.

Case XI was that of an extremely delicate girl whose percentage of lymphocytes was highest during the first week of the whoop. We notice here the high leucocyte count gradually decreasing as the case approaches convalescence. Two months after the cessation of the whoop the leucocyte count was 15,000 and the lymphocytes 50%, both above normal for a child of three.

In case XVII we also find a high leucocyte count and note how the lymphocytes gradually diminish and the polymorphs increase as the case improves until two months after the cessation of the whoop we get a normal count.

Case VIII was not so severe and there is little leucocytosis. During the first week of the whoop we find the lymphocytes to equal 80%, rapidly getting less and reaching the normal figure soon after the cessation of the whoop.

In case XXXIV the percentage of lymphocytes had reached the normal for that age before the whoop had quite disappeared and while there was still some leucocytosis.

So /

So far I have dealt with the lymphocytes in one group and we might now consider whether the so-called large lymphocytes and transitional forms are of any importance as regards the numbers present at different stages of the disease.

Stengel & White, (23) in three cases found from 17 to 27% of mononuclears.

Grulée & Phemister (28), and Bezançon & Labbé (14) all state that the large lymphocytes are increased in whooping cough, the latter considering them to be the characteristic feature of the disease. This is a difficult question to decide when there is no definite guide as to what is a large lymphocyte. I have previously pointed out that I draw a very hard and fast line as to what is and is not a large lymphocyte, and no doubt exclude many cells which some observers would class as large lymphocytes. In the cases observed by me there was not found any special increase of the large lymphocytes nor do I consider them to be an essential feature of the diagnosis.

In the great majority of the cases especially those with a high leucocytosis every variety of lymphocyte was met with. This was found to be the case by Stengel & White, who say that differentiation was difficult. Further it is impossible to rely for diagnosis on the numbers present of a particular variety of leucocyte when in the same film one observer /

observer might say he found 7% and another 14%.

Taking the average of each group we find the large lymphocytes to be more numerous during the later and chronic stages of the disease than during the early stages; they then exceeded the normal which Hutchison considers to be 8%. If I had not adopted such a rigid line of demarcation they would probably have exceeded the normal even more.

On looking through the counts individually we find the large lymphocytes (including the transitional forms) to vary from 3% to 20%, to occur quite irregularly and to have no definite bearing on the severity of the disease or the length of time it has existed. The fact however of a high percentage of large lymphocytes being present might be a factor in cases of doubtful diagnosis. Though a careful count was kept of the transitional forms, they were found not to be of any importance except as forming part of the class of large lymphocytes.

Eosinophiles.

Carriére (24) found the eosinophiles to vary from 12 to 15%--Boston of Philadelphia found them diminished or absent.

The latter statement I consider the correct one as I found the average percentage of eosinophiles at different stages of the disease to vary from /

from .6 to 3%. In many cases no eosinophiles were found in counting six to eight hundred leucocytes, while in a few the percentage of eosinophiles was 6 to 8%. This eosinophile increase was probably the result of some co-existing parasitic affection.

It is thus very evident that the principal factor in the blood of whooping cough patients is the relative proportion of Polymorphs and Lymphocytes present. There is undoubtedly an increase of the small lymphocytes, either absolute or relative, but for practical purposes it is simpler to consider all the lymphocytes in one group. The eosinophiles as I have pointed out are of no importance and the large lymphocytes per se. of very little importance. Meunier (21) was the first to point this out and observes that the proportion of polymorphs and lymphocytes is inverted. In the aggregate I find this to be true though individual cases vary greatly.

In table I we find the number of lymphocytes to considerably exceed the number of polymorphs, while in the following tables we find the number to be almost exactly inverted.

	Whooping Cough.		Normal, corrected for age	
Table	P.M.	L.	P.M.	L.
II	36	63	58	39
III	36	63	60	37
IV /				

Table Continued.

	Whooping Cough.		Normal, corrected for age.		
Table.	P.M.	L.	P.M.	L,	
IV	35	63.5	57	30	
V	34.8	64.6	55	42	
VI	43	54.6	55.5	42.5	

We find in each series of cases that the average number of lymphocytes considerably exceeds that of the polymorphs. Taking the cases individually we find in almost every case that the number of lymphocytes exceeds that of the polymorphs, and that this lymphocyte excess is more apparent in the severe than in the mild cases. Occasionally, however, one meets with a mild case with a high percentage of lymphocytes.

Carriére (24) found a Polymorph leucocytosis most marked in the early stages, and Koplik (26) one in the second week of the disease. This is entirely at variance with my observations and with those of Meunier &c, and is probably the result of some error of technique or to a printer's mistake.

Wanstall (25) found an increased percentage of lymphocytes at least equalling or exceeding that of the polymorphs, which my observations confirm.

Boston (29) found the lymphocytes to vary from 35 to 55%, which is considerably below the figures noted by me. We must remember however that there is /

is a normal lymphocytosis in infants; in cases of whooping cough we find this normal lymphocytosis much exaggerated, hence it is in infants that, as a rule, we get the highest percentage of lymphocytes.

COMPLICATIONS.

The most frequent complication met with in whooping cough is bronchitis, which was present in a number of my cases, two cases developed Broncho-pneumonia, one case was confined during the first week of the whoop, and one case developed Chicken Pox in the third week. These cases, except the last, are noted separately from the uncomplicated cases.

Bronchitis.

Before considering the influence of Bronchitis on the blood count of whooping cough, we must first decide what change, if any, is found in uncomplicated bronchitis.

Cabot (11) found the blood to be unaltered in chronic bronchitis, and in some cases of acute bronchitis. In 20 cases of acute bronchitis there was a leucocytosis exceeding 10,000 per C.mm. the highest being 68,000. One case of whooping cough with bronchitis gave a leucocytosis of 26,000.

The differential count resembled that of Pneumonia, /

Pneumonia, there being an increase of polymorphs.

DaCosta (13) says in Chronic Bronchitis leucocytosis hardly ever occurs and in acute bronchitis it is uncommon except when the finer tubules or vesicular structure are invaded; then a leucocytosis identical with Croupous Pneumonia is found.

Stengel & White (23) give the following counts of bronchitis occurring in children.

	Age	Lencocytes	P.M.	L.L.	S.L.	E.
J.H.	5	15,300	63.4	12.5	22.9	1.2
M.Mc.	4	19,226	74.7	11.2	12.9	1.2
L.G.	3	12,909	69.4	12.6	18	
T.W.	6	12,691	61.3	6.9	29.9	1.9
V.O.	3	14,507	87	9.4	3.6	
Average		14,926	71.1	10.5	17.4	.9

From these figures we see that, allowing for the age of the patient, there is a not very marked leucocytosis, that the polymorphs are increased, the small lymphocytes proportionately reduced and the large lymphocytes above normal.

Cases of acute whooping cough with bronchitis.

No.	Age	Lenco-cytes.	P.M.	L.L.	S.L.	E.	
XI	3yrs	68,800	24	9	66	1	1st week.
"	" "	55,000	47	8.5	44	.5	3rd "
XII	3mos	18,600	31	6.5	61.5	1	1st "
XVII	4½yrs	31,200	36	11	53		2nd "
XIX	2½ "	57,000	30	4	65	1	3rd "
XX	16mos	21,400	29	14	56.5	.5	3rd "
Average		42,000	33	8.8	58	.6	

Comparing this table with the preceding one, we note that there is a marked leucocytosis, that the Polymorphs are diminished and the small lymphocytes correspondingly increased and that the Large Lymphocytes are above the normal. Thus the increase of Lymphocytes due to the Whooping Cough more than counterbalances any Polymorph increase resulting from the Bronchitis.

The increase of Large Lymphocytes in both groups is probably the result of irritation of the Tracheo-bronchial lymphatic glands.

In cases of Whooping Cough with Bronchitis we find a much higher leucocytosis than in uncomplicated cases and in Table VIII among 5 cases with the highest leucocyte count, 4 of them have bronchitis. This high leucocytosis may be due however not to the /

the Bronchitis but to the severity of the Whooping Cough.

Broncho-pneumonia:

Only two cases developed pneumonia, both dying. Uncomplicated pneumonia causes a leucocytosis with an increased percentage of Polymorphs.
Stengel & White (23) quote Gundobin as finding the following average in six cases of pneumonia in children.
Lencocytes, 24,300; Polymorphs, 70%, Large Lymphocytes, 6%; Small Lymphocytes, 25%; Eosinophiles, 2.5%.

In 49 cases of Broncho-pneumonia Cabot found the majority of the counts to vary from 15,000 to 25,000; the Polymorphs being much increased, the Lymphocytes diminished, and the Eosinophiles absent. DaCosta confirms this.

Cases with Pneumonia:

Case XXXVIII Table XI age 16 months, was that of a previously healthy infant which had paroxysms of coughing, worst at night; other members of the family had whooping cough. The first count was made when the cough had lasted for two weeks, the only physical signs being those of acute bronchitis. There was then a Leucocytosis of 57,800 with 33% of Polymorphs, 64% of Lymphocytes and 1% of Eosinophiles. Five days later the child was found to have Pneumonia /

Pneumonia with dullness at the left base and was obviously very ill; there was no whoop. A count made then showed a Leucocytosis of 85,600 with 44% of Polymorphs and 56% of Lymphocytes. The differential count was very difficult as almost every variety of leucocyte was met with; many transitional and irregular forms were noticed as well as a few nucleated reds. The patient diéd the following day. A drawing from a film of this patient's blood will be found on the first page. In the second count the very high leucocytosis, the higher percentage of Polymorphs than in the first count and the absence of Eosinophiles were probably due to the Pneumonia. Though the Polymorphs were increased there was still a marked Lymphocytosis.

Case XX, age 7, did not come under my observation until during the sixth week of the disease when there had been a whoop for the previous three weeks. The child was very seriously ill, with consolidation of the right lung as high as the angle of the scapula and was unable to retain nourishment. The Leucocytes numbered 5,300 with 45% of Polymorphs 54% of Lymphocytes and .5% of Eosinophiles. A later count, made when the patient was in a state of collapse, gave a Leucocyte count of only 3,100. The patient died four days later. There was here a relative Lymphocytosis. The Leucopenia noted in

the last case can be accounted for by the severity of the Pneumonic infection overpowering the resistance of a patient already debilitated by a severe attack of Whooping Cough.

In the previous case the Pneumonia occurred at an early stage of the disease and the high leucocytosis marks a powerful reaction to a severe attack.

The most marked Lymphocytosis met with by Cabot (11), excluding leukaemia was in two cases of pneumonia in children. One, a child of six made an uneventful recovery from an attack of Bronchopneumonia, the only peculiarity being the marked increase of Leucocytes running up to 94,600, 69% of which were Lymphocytes. During convalescence the blood became normal. The other case, an infant, 15 months old, had paroxysms of coughing four days before admission, the Leucocytes numbered 103,000 with 64% of Lymphocytes and 35% of Polymorphs. The patient died on the sixth day and on the day before death the Leucocytes reached the enormous total of 185,000.! This case is very similar to the one noted by me, No. XXXVIII though the latter had not so high a Leucocytosis. Cabot after reading Meunier's paper considered both these cases to be atypical whooping cough.

Houston (34) in a discussion on the Rôle of the Lymphocyte at the Oxford Meeting of the British /

British Medical Association reported a case of Pneumonia in a child, 5 years old, with 10,000 Lymphocytes in a total Leucocyte count of 17,000. In his paper he says that "several similar instances have been noted by other writers as occurring in children. It seems necessary therefore to admit that the lymphocytes in young children may be increased in conditions which in the adult usually produce a pure polymorphonuclear increase. This argument is not complete and requires further proof."

DaCosta (35) remarks that "in the pneumonias of children the possibility of lymphocytosis should be remembered, for although a true lymphocytosis is rare it sometimes occurs." We note then in the cases reported by Cabot and myself that in Pneumonia occurring along with whooping cough, we get an absolute or relative lymphocytosis, and the tendency of the Pneumonia being to produce an increase of Polymorphs, the Lymphocytosis is not so marked as in uncomplicated whooping cough.

The cases of Pneumonia producing a lymphocytosis met with by Houston and DaCosta were probably cases of Whooping cough—Pneumonia,—the whooping cough being atypical.

Case XXXIV, table XII, this was a case observed during the puerperium.

The patient, age 34, had been coughing for three /

three weeks and was confined on the second day after the development of the whoop. The confinement was normal though there was rather more than the usual amount of haemorrhage. The blood was examined the following day and showed 19,600 Leucocytes per C.mm. with 82% of Polymorphs and 18% Lymphocytes. This is quite unlike anything met with in whooping cough but is the normal count for a patient on the first day after delivery.

During the later months of pregnancy and up till the time of delivery a Leucocytosis of the Polymorph type is usual, gradually falling to normal between the 5th and 10th day after delivery.

In this case on the 8th day after delivery the Leucocytes numbered 8,000 with 46% of Polymorphs and 54% of Lymphocytes. The whoop was now much less and the patient was convalescent. The second count is typical of whooping cough, but in the first one, the increase of Polymorphs resulting from the pregnancy and the considerable haemorrhage is sufficient to mask the Lymphocyte increase which we would expect from the whooping cough.

Chicken Pox:

One case, No III table V, developed chicken-pox during convalescence from whooping cough, causing a marked increase of both the large and small lymphocytes. Different observers give very contradictory /

contradictory reports as to the effect of chicken-pox on the blood count. We would expect to find a lymphocytosis from the envolvement of the lymphatic glands in Chicken-pox as in Small-pox. This was evidently the case here and in consequence we find a lymphocytosis more marked than is usually met with in convalescent whooping cough.

DIAGNOSIS

The question might be asked, can we put these observations to any practical use? I consider that we can, otherwise I do not think this thesis would ever have been written. Whatever will help the general practitioner in the early diagnosis of whooping cough or any other infectious disease is of the greatest value and I consider that by an examination of the blood in cases of suspected whooping cough we can make a positive diagnosis.

Any mother can diagnose whooping cough after the characteristic cough has appeared, but can any Medical Man do so before then or in atypical cases where there is no whoop? He may have his suspicions but to isolate a family on suspicion alone is to assume a great responsibility, especially in such a disease as whooping cough where the characteristic symptoms are often late in developing. In atypical cases a definite diagnosis may never be reached. This question has a personal interest because while at a boarding school, two of my brothers and myself were isolated for some weeks on account of a suspicious cough which puzzled various medical men who were consulted and led to a variety of diagnoses. As the typical whoop never developed the unpleasant quarantine was finally relaxed, the question /

question of whooping cough or not whooping cough never being decided. How much more satisfactory would it have been, if an examination of the blood could have been made and a definite diagnosis given. Then either the isolation would have ceased or it would have been maintained on a certainty and recognised to be necessary.

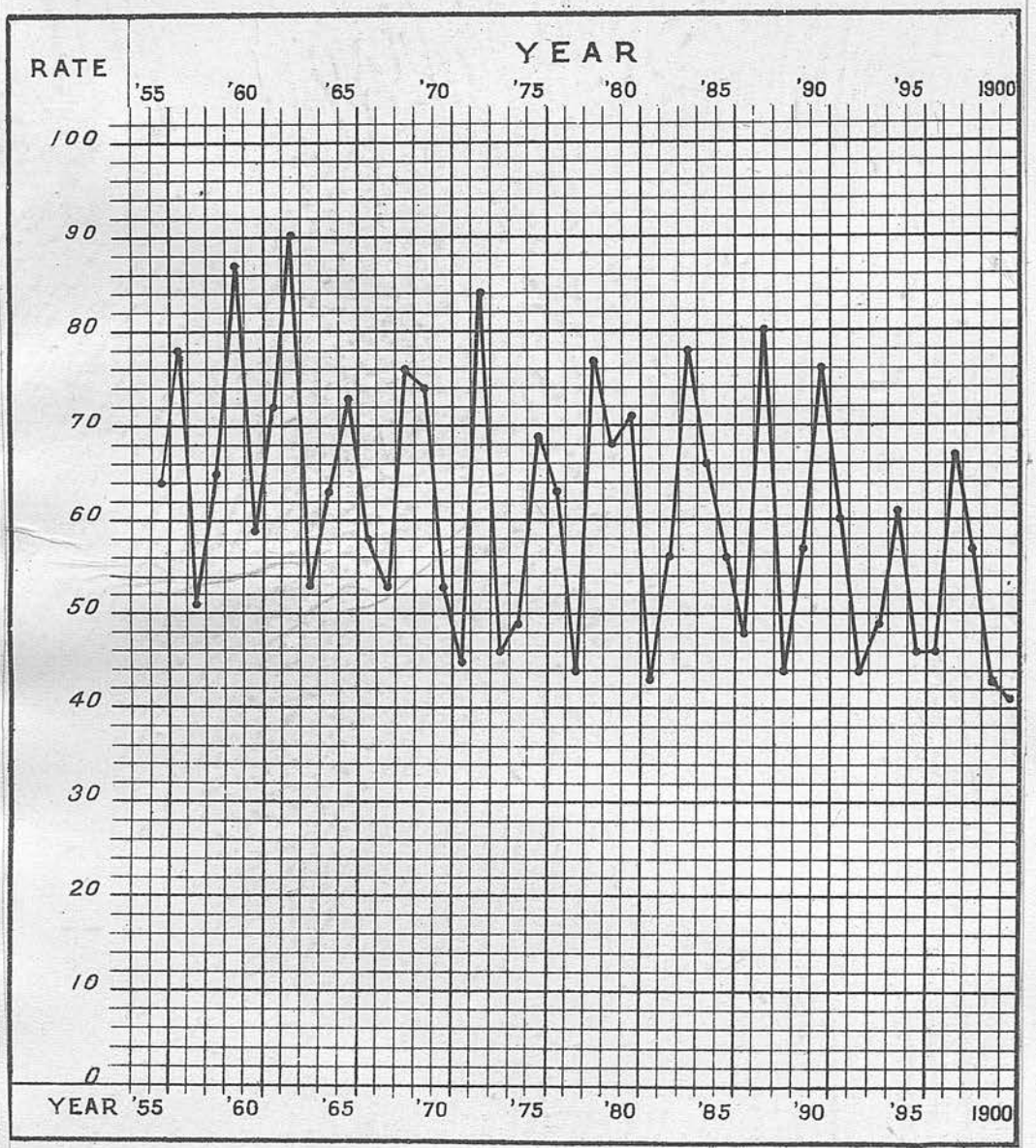
Weill & Péhu (36) consider the contagious period of whooping cough to be during the catarrhal stage and that it rapidly lessens as the characteristic cough develops. If this is proved to be correct, it causes the early diagnosis of whooping cough to be of the greatest importance and proves that isolation as at present adopted is too late to be of much use in preventing the spread of the disease. The comparative inutility of isolation in epidemics of whooping cough is recognised by all who have had much experience of this disease.

Fagge & Pye Smith say that as a rule in the early stages of whooping cough there is no means of diagnosis or even of suspicion.

Osler, Taylor and other writers on Medicine and the diseases of children all agree as to this difficulty of diagnosis. Only by a few American authors is the value of an examination of the blood recognised.

CHART No. 8.

DEATH RATE PER 100,000 FROM HOOPING-COUGH, 1855 TO 1900.



The chart on page opposite, gives the deathrate from Whooping cough in Scotland from 1855 to 1900. It shows that the deathrate is higher than that of Measles, Scarlet fever or Diphtheria and proves Whooping Cough to be one of the most fatal maladies of early childhood. We note also that the deathrate has diminished but little during later years unlike other Zymotic diseases. Might we not hope for a reduction of this high deathrate if vigorous isolation could be adopted earlier as the result of more certain methods of diagnosis.

The Value of Leucocytosis in Diagnosis.

Meunier (21) says that "a leucocytosis is invariably present in cases of whooping cough and that it is always notably higher than that which is met with in other nonfebrile affections of the respiratory system; its early appearance before the typical convulsive cough gives it a real importance in cases of doubtful diagnosis, and a valuable help in prophylaxis,"

De Amicis & Pacchioni (22) consider the constancy of this leucocytosis to be a valuable aid in diagnosis when prophylaxis may yet be possible.

Boston(29) affirms that whooping cough is the only example of an afebrile disease affecting the respiratory tract where leucocytosis is a constant symptom. /

symptom.

In cases in the catarrhal stage I found in all a leucocytosis sufficiently high to be quite distinctive.

Wanstall in 8 cases found the count to vary from 4,600 to 34,000.

In my analysis of cases during the first three weeks of the whoop the majority were found to have a decided leucocytosis but some, in patients over five years old with a mild attack, showed little or no leucocytosis. In these cases the characteristic cough made the diagnosis easy but if they had been atypical, a diagnosis from the total leucocyte count alone would have been impossible.

In pneumonia and in some cases of acute bronchitis we get a leucocytosis but here the physical signs should be sufficient for diagnosis, one must always remember however that they may occur as complications of whooping cough. No leucocytosis is found in acute miliary tuberculosis, tubercular adenitis, pleurisy or pulmonary phthisis nor in bronchial catarrh, measles or influenza, so long as these diseases are uncomplicated by any secondary process, This absence of Leucocytosis would be sufficient to distinguish these diseases from whooping cough. In examining the blood of a patient suspected to have whooping cough care must be /

be taken to exclude the many septic, infectious and toxic conditions which produce a Leucocytosis, as well as the physiological leucocytosis met with in pregnancy. In the later stages of whooping cough some mild cases are met with which do not show a leucocytosis so that a normal count or one only slightly above normal is not sufficient by itself to exclude whooping cough.

The Value of a Differential Count in DIAGNOSIS.

Lymphocytosis has been defined as an absolute or relative increase in the lymphocytes above the number normal in health. In whooping cough we find this increase of lymphocytes and the lymphocytosis of whooping cough would have been a more correct title for this thesis than Leucocytosis. Leucocytosis however is the term used by other writers and as in some cases of whooping cough the lymphocytosis is only relative it is perhaps better not to use the latter term to indicate what is really a diminution in the number of Polymorphs.

Meunier says that the Proportion of lymphocytes and polymorphs is inverted, which my observations confirm, and that in cases with a leucocytosis above /

above 30,000 the lymphocytes are quadrupled.

Stengel & White found an invariable lymphocyte increase.

Wanstall in 18 counts found a percentage of lymphocytes at least equalling or exceeding the number of leucocytes.

Grulee & Phemister state that the lymphocytes are relatively increased at all stages of the disease; DaCosta that lymphocytosis is a characteristic finding in whooping cough.

In 82 differential counts made in typical cases of whooping cough, acute and chronic and at all stages, I find 72 with a percentage of lymphocytes equal to or exceeding that of the polymorphs, 60 having an absolute and 12 a relative lymphocytosis . Of the remaining 10, in 4 there was a lymphocytosis as they had all less than 55% of polymorphs, though the percentage of polymorphs was greater than that of the lymphocytes, so that we have 76 counts out of 82 showing a lymphocytosis .

Of the other six, four were chronic cases of over four months duration and had from 62% to 74% of Polymorphs, though there was a leucocytosis of from 14,000 to 23,000. It is not however in these very chronic cases that a definite diagnosis is of importance, but in the earlier stages of the disease at which period I only found two cases which did not show /

show a lymphocytosis. One age 5, (case XXII) had a leucocytosis of 12,000 with 68% of Polymorphs. The patient had been ill for over five weeks and was then convalescent with very little whoop, and the count here shows that the blood may return to normal before recovery is complete. We have now only one doubtful case to account for and that is No.VII a previously strong and healthy boy age 7, in the first week of the whoop. He had a count of 18,000 leucocytes with 68% of Polymorphs, and 31% of Lymphocytes This count was most exceptional and may have been due to faulty technique though several films were examined and 600 leucocytes counted in each, the different counts being practically identical. The leucocytosis would here lead to a suspicion of whooping cough. A later count made of this case showed 32% of Polymorphs and 66% of LYmphocytes.

Excepting the above case in all the counts made in the acute stages of whooping cough both mild and severe we find a lymphocytosis and in the great majority of cases the number of lymphocytes exceeds or is equal to that of the polymorphs.

It is this lymphocytosis which is the essential feature in the diagnosis of whooping cough and distinguishes it from all other diseases with a cough. The only other disease where a similar condition of the blood is found, is small-pox.

In lymphatic leukaemia the lymphocytosis is so enormous /

enormous as to easily distinguish it from whooping cough. We may get a relative lymphocytosis in some cases of chlorosis, sarcoma of the lymphatic structures, pernicious anaemia and chloroma but here the clinical symptoms would be sufficient to distinguish them from whooping cough.

In young children debilitated by rickets, scurvy hereditary syphilis or chronic diarrhoea, a relative lymphocytosis may be met with considerably less however than that met with in whooping cough. Should such cases develop whooping cough we would get an absolute lymphocytosis higher than that usually met with in uncomplicated whooping cough.

Diseases with a cough likely to be mistaken for whooping cough are tubercular or syphilitic enlargement of the tracheo-bronchial lymphatic glands, of these conditions Cabot says, "In tuberculous adenitis the blood is either normal or anaemic if the cachectic state of the patient is marked, or should there happen to be a secondary infection of the glands plus the tuberculous lesions, a simple polynuclear leucocytosis is found.

In syphilitic adenitis there is often anaemia with a moderate polynuclear leucocytosis and with a relative lymphocytosis especially in children,"

In adults some forms of debility may be associated with a relative increase of lymphocytes; whooping cough however is rare in adults and the only case I observed had a much greater lymphocytosis than /

than could be the result of debility.

In acute bronchitis with leucocytosis, and in uncomplicated pneumonia we find a polymorph increase In cough due to measles, bronchial catarrh, nervous affections &c, we find a normal differential count.

It has been thought by some authorities that the large lymphocytes are an essential feature in the diagnosis. As I have previously pointed out I do not consider there is sufficient evidence to warrant this assertion. It is true that in some cases of whooping cough we do get an increase of the large lymphocytes but Houston (34) has found a similar increase in a great variety of diseases. He has published statistics showing that in many cases of chlorosis, pernicious anaemia, enlarged spleen, glandular enlargements due to sarcoma &c, tubercle, typhoid &c, and in many septic conditions, the large lymphocytes may vary from 10 to 35%.

In doubtful cases where the lymphocytosis was not very marked an unusually high percentage of large lymphocytes would point very strongly to whooping cough provided there were no evident glandular enlargement. From the examination of the blood of patients with a cough, I consider that we can positively diagnose whooping cough if we find:--

(1) Lymphocytosis, absolute.

(2) Lymphocytosis, relative, the number of lymphocytes being equal to or exceeding the /

the number of polymorphs.

(3) Lymphocytosis, relative; the percentage of polymorphs being below normal though exceeding that of the lymphocytes, and the large lymphocytes above normal.

We can exclude whooping cough if we find the polymorphs to be normal or above normal.

The case would be doubtful should the polymorphs be below normal, the lymphocytes only slightly increased and the large lymphocytes not above normal. A negative diagnosis should not be given especially should any leucocytosis be present until a second count has been made after an interval of four days.

Having thus formulated certain rules for our guidance in diagnosis we might now examine table VII where we have counts made in a number of cases which never developed the characteristic whoop and endeavour to ascertain if these are cases of atypical whooping cough or not.

Case XXXVI age 5 had suffered from a chronic cough for eight weeks and suspecting whooping cough I made an examination of the blood. There was a leucocytosis of 11,200 with 61% of Polymorphs and 30% of Lymphocytes. The percentage of Polymorphs was normal for a child of 5, but the leucocytosis was suspicious as well as an increased percentage of Large Lymphocytes. A later count cleared /

cleared up the diagnosis as there was then found only 37% of Polymorphs and 59% of Lymphocytes--a count quite characteristic of whooping cough.

Case XXXVII, age 10 had suffered from a cough for three weeks, worst at night. A count here showed a leucocytosis of 16,600 with 36% of Polymorphs, 54% of small Lymphocytes and 9% of large Lymphocytes. This was undoubtedly a case of whooping cough.

Case XXXVIII. This case has been previously referred to under the complications of whooping cough. There had been cough for two weeks, pneumonia supervened and the child died in a few days. This was certainly a case of whooping cough there being 67% of Lymphocytes.

Case XXXIX. This patient age 7, had coughed for a fortnight and had a leucocytosis of 11,000 with 46% of Polymorphs and 51% of Lymphocytes; evidently a mild case of whooping cough.

A later count showed 52% of Polymorphs and 50% of Lymphocytes out of a total of 5,000 leucocytes. The patient was then much better though still coughing.

Case XL. age 7, had coughed for 3 weeks. There was a total leucocyte count of 18,400 with 81% of Polymorphs and 18% of Lymphocytes. This was certainly not whooping cough though the leucocytosis was /

was suspicious and not easily accounted for except as the result of digestion.

Case XLI. age 3, with cough for 3 weeks had a leucocyte count of 10,500 with 60% of Polymorphs and 41% of Lymphocytes. This was certainly not whooping cough.

The next two cases were brothers who had suffered from a suspicious cough for three weeks for which there was no evident cause and I was consulted as to whether it would be safe for them to attend a Sunday School treat. As the original epidemic had been started by an unsuspected case in the catarrhal stage attending a similar function a definite diagnosis of the above cases was of importance.

Case XLII, age 5½, had a leucocytosis of 12,400 with 57% of Polymorphs, 30% of Small Lymphocytes and 15% of Large Lymphocytes. This was not a very definite count but the leucocytosis together with the high percentage of large lymphocytes decided me in favour of whooping cough. Another factor in the decision was that the other brother, age 3½, case XLIII had a more typical count, 11,300 leucocytes with 48% of Polymorphs, 37% of Small Lymphocytes and 15% of Large Lymphocytes.

In the last case there was a leucocytosis, the number of Lymphocytes exceeded the number of Polymorphs and there was an abnormally high per-

centage /

percentage of Large lymphocytes, all characteristic of whooping cough. Both cases were isolated and rapidly recovered. An early diagnosis besides being valuable in prophylaxis renders possible vigorous treatment before the disease has developed and I think that in consequence some of the cases were aborted.

The treatment which I found most effective in cutting short the attack at an early stage was the administration of eu-quinine in fairly large doses.

GENERAL CONCLUSIONS.

So far I have dealt only with the facts which are apparent in observations on the blood of whooping cough patients, and I now propose to consider what inferences we can draw from them. Such inferences can at the best be only theoretical and must remain so until we have a fuller knowledge of lymphocytosis and its relation to pathogenic organisms.

The clinical history of whooping cough points strongly to the existence of a specific organism to which the catarrhal and nervous symptoms may be more or less attributed, but so far pathologists have not determined with certainty the exact micro-organism. According to Cheney (37) the 1st or catarrhal stage means the presence and growth of the specific germ upon the laryngeal and tracheal mucous membrane. The 2nd or paroxysmal stage that the germ has developed virus sufficient in amount to affect the nervous system, and the 3rd stage the gradual eliminating from the system of the toxic products of the germs.

Leucocytosis is essentially a new formation of leucocytes and in infectious diseases represents Nature's attempt to rid the blood and the system by means of leucocytes and their products, of the bacterial and toxic causes of disease.

Pathological Lymphocytosis may be interpreted as indicating a response to disturbances of lymphoid tissue /

tissue by toxic agencies.

A discussion on the "Rôle of the Lymphocyte" at the Oxford Meeting of the British Medical Association contains much interesting and valuable information on the subject of lymphocytosis.

No one now doubts the origin of lymphocytes from lymph glands and lymphatic tissue generally and as in children this lymphoid tissue is widely distributed and specially abundant, this pathological lymphocytosis is of the greatest importance in the diseases to which they are subject.

Gulland (16) points out that the main depôts of lymphocytes apart from lymph glands and marrow are round the hollow tubes of the body, the alimentary and respiratory tracts and that these are the places which are occupied by saprophytic, non-virulent and attenuated organisms. He considers that lymphocytes are sufficient to keep these in check though they may not be able to resist virulent infections.

Ehrlich (38) attributes lymphocytosis to the local irritation of certain areas of lymphatic glands which produces an increased circulatory activity in these situations in consequence of which large numbers of lymph elements are swept mechanically from the lymphatics and enter the general circulation.

More recent researches by Wolff, Hirschfield (39), Wlassow & Sep (40), Ewing (12) and others prove /

prove the existence of Amoeboid movements to a certain extent, in the lymphocytes.

We have thus two methods of lymphocytosis, the mechanical of Ehrlich, and the chemiotactic of Wolff and others. They are not necessarily conflicting views as both may be, and probably are, true.

Pathological lymphocytosis may be divided into two classes;

1st, relative and slight, where there is a reduction of the polymorphs as well as an increase of the lymphocytes e.g. lymphosarcoma, Hodgkin's disease and some cases of tuberculous and syphilitic adenitis.

2nd, absolute and marked e.g. Small-pox, Whooping cough and Lymphatic Leukaemia. It is possible that the lymphocytosis occurring in the first group is the result of purely mechanical processes. Houston (34) considers this to be the case in tubercular and syphilitic affections where the specific toxins have the power of gathering large numbers of lymphocytes to the pathological focus.

The lymphocytosis in this first group may however not be entirely mechanical as in some cases it is at the expense of the large lymphocytes which from their larger amount of protoplasm possess more amoeboid /

amoeboid movement than the small lymphocytes.

In the 2nd group the lymphocytosis is too great to be explained on merely mechanical grounds and one must regard it as an active, chemiotactic process.

An active lymphocytosis is rare in any other disease though Houston reports two cases where it was found. One was a case of chronic phosphorous poisoning where there was a very considerable increase of the lymphocytes as well as of the polymorphs. We can here see no definite reason why the polymorph increase should be regarded as an active process and the increase of the lymphocytes as a purely passive phenomenon since the mixed leucocytosis was the result of a definite poison.

The other case was one of acute croupous pneumonia in a man of 54. The sputum was full of pneumococci and the blood instead of showing a polymorph increase presented a picture closely resembling lymphatic leukaemia. There was a total leucocyte count of 94,000 per C.mm. of which 84,000 were lymphocytes. It seems difficult to explain such a case except on the assumption that the lymphocytes were influenced by the toxin instead of the polymorphs as is usually the case in pneumonia. If it were not for the age of the patient we might suspect this to be a case of whooping-cough-pneumonia. Lymphatic Leukaemia may be the result of a toxin possibly elaborated by a specific micro-organism.

Moorhead, /

(Moorhead (41)) The enlargement of the lymphatic glands would then be due to the direct action of the toxin within them, the glands acting as filters.

In small-pox according to Ferguson (42) a very high proportion of lymphocytes is found in the blood and in the skin. There is also a high degree of cellular activity in the lymph glands, and the lymph sinuses and periglandular connective tissue are crowded with lymphocytes. In view of the fact that the presence of small-pox in the skin excites there an exudation composed largely of mononuclear cells of the lymphocyte class and that the virus is conveyed from the skin to the superficial lymphatic glands, it may justly be inferred that the proliferative activity of the lymphoid cells in the glands is the direct result of the virus.

I consider that we have thus good reasons for believing that the lymphocytosis of Whooping cough is also due to a positive chemiotaxis, the result of stimulation of the lymphoid tissue by the specific germ or its toxins. This specific germ is believed to grow upon the mucous membrane of the respiratory tract during the catarrhal stage and it is then that the lymphocytes are found to be most numerous. This results in enlargement of the tracheo-bronchial lymphatic glands and increased cellular activity of the /

the neighbouring lymphatic tissue producing an increase of lymphocytes which attempt to destroy the invading organism and to counteract its noxious influences. This they do either by acting as phagocytes or from the faculty they possess of producing certain chemical substances (alexins) which are either directly bactericidal or act as antitoxic agents. Should the lymphocytes gain the mastery then the attack is aborted or at any rate runs a mild course and may be atypical, the characteristic whoop not developing. A severe and typical attack indicates that the specific germ has been able to overcome the resistance of the lymphocytes, the toxins resulting, being the cause of the typical nervous symptoms.

The reason why in whooping cough we get a lymphocytosis and not a polymorph increase may be that the specific germ is not very virulent and can be dealt with by lymphocytes which are undoubtedly phagocytic. Again whooping cough is a disease of children where the lymphoid tissue is specially abundant. The specific germ apparently grows on the mucous membrane of the respiratory tract and elaborates a toxin which the lymphocytes may be specially able to counteract by the formation of an antitoxin.

According to Bezancon & Labbé (14) this increase of /

of lymphocytes generally gives a permanent protection It is certainly very unusual for a patient to have a s second attack of whooping cough.

In conclusion I think that this is a subject well worthy of further investigation. I regret that I have not more cases to record or more counts of those cases that I did see, but the epidemic had begun to decline before I commenced my investigations and it unfortunately occurred during the height of the season when a Medical Man has but little time to spare for the detail required in blood examinations.

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BIBLIOGRAPHY.

(1) Coles "The Blood" 1905 p.22.

(2) Wharton Jones "Phil Transactions" London 1846.

(3) Max Schultze "Arch.f. Mikr. Anat" Bonn. 1865.

(4) Ehrlich "Verhandl. d. physiol. Gesselloch. Zu Berlin" 1878 - 79.

(5) Hayem "Du Sang" Paris 1889.

(6) Muir "Journal Anat. and Physiol" London 1891.

(7) Metchnikoff "L'Inflammation" Paris 1892.

(8) Kanthack & Hardy "Journal of Physiology" 1894.

(9) Coles "The Blood" 1905, p 69.

(10) V.Limbeck "Clinical Pathology of the Blood" 1901.

(11) Cabot "Clinical Examination of the Blood" 1903.

(12) Ewing "Clinical Pathology of the Blood" 1904.

(13) DaCosta "Clinical Hematology" 1905.

(14) Bezançon & Labbé "Traite d'Hematologie" 1904.

(15) Scott "Journal of Pathology & Bacteriology" January 1906.

(16) Gulland "British Medical Journal" September 10th 1904, p. 583.

(17) Houston "British Medical Journal" September 10th 1904, p. 591.

(18) Rotch "Pediatrics" Philadelphia, 1896, p. 342.

(19) Hutchison "Lancet" May 7th, 1904.

(20) Frohlick "Jahrbuck f. Kinderh" Vol XLIV No.1 p. 53.

(21) Meunier "Archiv. d. Maladies de l'enfance" April, 1898.

(22) De Amicis & Pacchioni "Clin. Med. Italian" 1899
"Revue Mensuelle des Maladies de l'enfance"
January, 1900.
(23) Stengel & White. "Archiv. Pediatrics" 1901 Vol XVIII
p.p. 241 & 321.
(24) Carrière "Soc. de Biologie" Feb. 1st, 1902.
(25) Wanstall "American Medicine" Jan 1903 p. 63.
(26) Koplik "Diseases of Infancy and Childhood"
New York, 1903.
(27) Chalmers Watson "Encyclopedia Medica" 1903.
(28) Grulée & Phemister "Archives of Pediatrics,
1905 p. 595.
(29) Boston "Textbook of Clinical diagnosis" 1905.
(30) "International Clinic" 1905 Vol IV p. 230.
(31) DaCosta "Clinical Hematology" 1905 p. 502.
(32) Cabot "Clinical Examination of the Blood" 1902
p.p. 218 & 195.
(33) Bezançon & Labbé. "Traite d'Hematologie" p. 562.
(34) Houston ? "British Medical Journal" Sept 10th 1904
p. 593.
(35) DaCosta "Clinical Hematology" 1905 p. 510.
(36) Weill & Péhu "La Semaine Medicale" Nov 27th 1901
p. 385.
(37) Cheney "Cyclopedia of the Diseases of children"
Vol. V. p. 259.
(38) Ehrlich & Lazarus "Die Anaemie" 1900.
Nothnagel's spec. path. v. Therap Vol VIII No 2.
(39) Hirschfield "Berl. Klin. Woch." 1901.
(41) Moorhead "British Medical Journal Sept 10th 1904.
(42) Ferguson " " " " " "